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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,256	09/13/2005	Angus Moodycliffe	112701-818	3290

29157 7590 12/22/2009

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EXAMINER
SHIN, DANA H

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
12/22/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chicago.patents@klgates.com

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/525,256	**Applicant(s)** MOODYCLIFFE ET AL.	
	Examiner DANA SHIN	**Art Unit** 1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 December 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): 102(a), 102(b), 102(e) rejections.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *6 and 7*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

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/Dana Shin/
Examiner, Art Unit 1635

Continuation of 11. does NOT place the application in condition for allowance because: applicant's arguments are not persuasive to demonstrate that claims 6-7 were fully enabled at the time the application was filed. Applicant has merely stated that working examples are not required to comply with the enablement requirement. Applicant is partially correct in that working examples per se are not required to determine whether a claim is enabled. However, the presence/absence of working examples is not the only factor that is considered when determining patentability of a claim under 35 U.S.C. 112, first paragraph. As repeatedly stated in the prior Office actions, neither the state of the art nor the instant specification teaches the required nexus between RNA antisense-mediated glucosylceramide synthase mRNA inhibition and epithelial tissue damage treatment/prevention. Note that the amount of guidance or direction needed to enable the invention is INVERSELY related to the amount of knowledge in the state of the art as well as the predictability in the art. See MPEP 2164.03: "if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling." Although working examples commensurate in scope with the claims are not required for enablement requirement purpose, the specification must provide sufficient amount of information and guidance pertaining to the claimed invention to be enabling, especially if the knowledge and state of the art pertaining to the claimed invention were not sufficiently established at the time of filing. In the instant case, there is no single prior art of record that shows, demonstrates, or describes the functional role of glucosylceramide synthase mRNA that causes any epithelial tissue damage, nor does the instant specification shows such functional role. Again, as repeatedly stated in the prior Office actions, the claimed nexus (inhibition of glucosylceramide synthase mRNA and treatment/prevention of epithelial tissue damage) is merely based on inventors' own deductions and speculations without any scientifically supporting evidence. As such, the complete lack of working examples commensurate in scope with the claims, or the lack of a working example actually showing that inhibition of glucosylceramide synthase mRNA results in treatment/prevention of a single epithelial tissue damage contributes to the final determination that an undue amount of experimentation would have been required for one of ordinary skill in the art to make the claimed composition and use the composition to treat and prevent any type of epithelial tissue damage including but not limited to scars, tissue inflammation, psoriasis, burns, and epithelial tissue cancer that is not limited to the skin eptithelial tissue but includes kideny epithelial tissue, brain epithelial tissue, and lung epithelial tissue. Furthermore, the enablement issue with the claim language "preventing" and "prevents" (see the dictionary citation of record) remains unresolved, and applicant has not pointed out how the claimed RNA antisense compound is able to stop any and all types of epithelial tissue damage from occuring (see the definition of the word "prevent" in the dictionary citation of record).

Applicant further argues that the claimed invention is sufficiently described in the specification by pointing out pages 2 and 4 of the specification. First, it is noted that the page nubmers indicated by applicant do not correspond to either the PCT specificaiton or the US specification. Second, the mere "statements" such that glucosylceramides (not glucosylceramide synthase) are involved in "normal skin homeostasis" do not whatsoever show that inhibition of glucosylceramide synthase mRNA results in therapeutic/preventative effects for any type of "epithelial tissue damage" as broadly and generically claimed in the instant case, wherein the damage includes brain epithelial tissue damage such as brain carcinoma. Simiarly, the mere statement that "glucosylceramide synthase"-mediated ceramide glycosylation is involved in epithelial carcinoma resistance does not whatsoever teach that inhibition of glucosylceramide synthase mRNA treats and prevents any and all types of epithelial tissue damage. Furthermore, there is no prior art reference incorporated in the specification for the alleged "well established" knowledge pertaining to the role of glucosylceramide and epithelial carcinomas (note that paragraph 51 states "It is well established that ceramide glycosylation, via glucosylceramide synthase, and the subsequent build up of glucosylceramides allows cellular escape from stress-induced programmed cell death, conferring cancer cell resistance"), nor has applicant ever submitted a prior art reference showing the DIRECT relationship between glucosylceramide synthase inhibition and treatment/prevention of epithelial tissue damage or the DIRECT relationship between glucosylceramide synthase mRNA upregulation and resultant epithelial tissue damage.

Applicant argues that working examples showing CD1d expression reduction and reduced skin irritation are sufficient to show that the claimed invention was fully enabled. Contrary to applicant's argument, as EXPLICITLY stated and admitted by the inventors of this appilcation, the alleged correlation between reduced CD1d expression/activity and reduced glucosylceramide synthase is merely based on inventors' speculations as evidenced by the statements in paragraph 51 pointed out by applicant: "it is ENVISIONED" that "POSSIBLY at the level of protein-glucosylceramide binding", CD1d regulates cancer cell resistance (emphasis added). Hence, as clearly acknowledged by the inventors of this case, again, the alleged functional role of the instantly claimed target gene (glucosylceramide synthase) in causing any epithelial tissue damage and the asserted consequence of treatment/prevention of any epithelial tissue damage with an RNA antisense targeted to glucosylceramide synthase mRNA are merely a possible, theoretical idea "ENVISIONED" (emphasis added) and speculated by the inventors of this application, and thus such required knowledge/information was not scientifically proven by the inventors of this case, and furthermore, no prior art taught the required association between glucosylceramide synthase and epithelial tissue damage.

In view of the foregoing, it is concluded that the specification fails to teach that the claimed antisense compound is able to treat, let alone prevent, any given epithelial tissue damage within the generic breadth encompassing myriad speices of epithelial tissue damage, and therefore, claims 6 and 7 remain rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement.